

**REMARKS**

Entry of the foregoing, reexamination and reconsideration of the subject application are respectfully requested in light of the amendments above in the comments that follow. By the present Response, Claims 16 is amended to include the limitation of Claim 18. Thus, upon entry of the present Response, Claim 16 – 17, 19 – 31 are pending and await further consideration on the merits.

**CLAIM REJECTIONS UNDER OBVIOUSNESS-TYPE DOUBLE PATENTING**

Examiner provisionally rejected Claims 16 – 31 on the grounds of nonstatutory obviousness-type double patenting over Claims 1 – 13 of U.S. Application No. 10/522,234 (“the ‘234 application”) and Claims 1 – 13 of U.S. Application No. 11/583,940 (“the ‘940 application”).

The Examiner alleges the instant claims are not patentably distinct because the ‘234 application is to microcapsules having a core comprising an active agent and a solubilizing agent, each surrounded by a coating made of two types of polymers, plasticizers and lubricants.

Applicant’s representatives (“Applicant”) respectfully disagree with the rejection. The claims of the ‘234 application do not disclose, teach, or suggest use of at least one solubilizing agent in the core of a microcapsule, wherein the at least one solubilizing agent is capable of increasing the solubility of the at least one active principle by more than 50% when the at least one solubilizing agent is placed in an aqueous solution at a concentration of 20% w/w at 37°C; and wherein the at least one solubilizing agent confers properties upon the core such that in a dissolving test (TD) a non-coated core releases 80% of the at least one active principle in less than two hours. As such, Applicant respectfully requests the Examiner withdraw the double patenting rejection.

The Examiner also alleges the instant claims are not patentably distinct from the ‘940 application. Applicant notes the ‘940 application also does not teach the required element of at least one solubilizing agent in the core of a microcapsule, wherein the at least one solubilizing agent is capable of increasing the solubility of the at least one active principle by more than 50%

when the at least one solubilizing agent is placed in an aqueous solution at a concentration of 20% w/w at 37°C; and wherein the at least one solubilizing agent confers properties upon the core such that in a dissolving test (TD) a non-coated core releases 80% of the at least one active principle in less than two hours. As such, Applicant respectfully requests the Examiner withdraw the double patenting rejection.

### **REJECTIONS UNDER 35 U.S.C. § 102**

Claims 16-26 and 28-31 are rejected under 35 U.S.C. § 102(b) as being anticipated by Mehta (U.S. Patent 5,084,278). Applicants respectfully traverse this rejection for the reasons detailed below.

The instant specification and claims are to a specific oral pharmaceutical formulation.  
Amended Claim 16 is to:

Orally administered microcapsules for modified release of at least one active principle with low solubility,  
wherein the mean diameter of the microcapsules are less than 1000 microns;  
wherein each microcapsule has a core comprising at least one active principle and at least one solubilizing agent,  
wherein the at least one solubilizing agent is capable of increasing the solubility of the at least one active principle by more than 50% when the at least one solubilizing agent is placed in an aqueous solution at a concentration of 20% w/w at 37°C;  
wherein the at least one solubilizing agent confers properties upon the core such that in a dissolving test (TD) a non-coated core releases 80% of the at least one active principle in less than two hours;  
wherein the core is coated with a coating film which controls the modified release of the active principles;  
wherein the coating film is at least 3% dry weight/dry weight of the microcapsule mass;  
wherein the coating film of each microcapsule comprises at least one film-forming polymer (P1) insoluble in gastrointestinal tract fluids, at least one water-soluble polymer (P2), and at least one plasticizer, (PL).

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v.*

*Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). Applicant submits, however, that Mehta does not anticipate the instant claims because Mehta does not teach each and every element of the claim.

The Examiner alleges that Mehta teaches coating compositions comprised of both a high temperature film forming polymers and low temperature film forming polymer, where the preferred high temperature film forming polymer “can be ethyl cellulose . . . that since the same polymer is used with the active agent in the core, it should be capable of increasing the solubility of the at least one active principle by more than 50% as required by instant claim 1.” Office Action at 4. Applicant respectfully disagrees for several reasons.

First, Applicant notes that Mehta pulled ethyl cellulose from a laundry list, where ethyl cellulose is used as a *diluent* in the core. Office Action at 4. This has no bearing on the present claims, because the invention is to use of ethyl cellulose as an element of the coating, and is not used in the core. Further, ethyl cellulose is not a solubilizing agent.

It appears the Examiner believes a diluent and a solubilizing agent are interchangeable. Applicant respectfully disagrees: a *diluent* is not the same as a *solubilizing agent*.

The solubilizing agent of the instant specification is described as “having the particularity, as soon as it is placed in aqueous solution at a concentration of 20% w/w at 37°C, of increasing the solubility of the AP by more than 50%.” See, specification at ¶41. Indeed, the only solubilizing agents present in the instant specification are those selected from hydrophilic polymers, surfactants and sequestering agents. See, *Id.* at ¶55 – 63. Furthermore, solubilizing involves “mak[ing] a substance such as a fat or lipid soluble or more soluble, especially in water...” See, American Heritage® Dictionary of the English Language, 4<sup>th</sup> Edition, 2000. Indeed, the solubilizing agents of the instant specification are all substances that make fats or lipids more soluble in aqueous solutions, including hydrophilic polymers, surfactants, and sequestering agents.

In contrast, a diluent is “an inert substance used to dilute.” See, *Id.*

There is no evidence that a diluent is a *prima facie* solubilizing agent, as suggested by the Examiner on page 3 of the Office Action. Further, as a common dictionary demonstrates, the characteristics of a solubilizing agent and a diluent are dissimilar.

Second, there is no evidence in Mehta that use of ethyl cellulose in the core would work as to increase the solubility of the active principle. In fact, as the instant specification and claims state, ethyl cellulose is water-insoluble. *See*, instant specification at ¶86, Claim 21. To Applicant's knowledge, there is no evidence that ethyl cellulose would work as a solubilizing agent. Moreover, the Applicant does not claim use of ethyl cellulose as solubilizing agent. Instead, the Applicant has both discussed and claimed ethyl cellulose as being water-insoluble, and thus appropriate as a film forming polymer P1. *Id.* Further, there is no evidence in Mehta of how a water-insoluble compound such as ethyl cellulose can be a "solubilizing agent." Thus, the Office lacks the evidentiary support to shift the burden to the Applicant.

In addition, Applicant submits that the Examiner is picking and choosing from different portions of Mehta and adding the Examiner's own hindsight, which does not constitute anticipation, nor does it in any way demonstrate each element of the instant claims. Further, Applicant notes that for a reference to anticipate, the "elements must be arranged as required by the claim." *See*, MPEP 2131 (citing *In re Bond*, 910 F.2d 831 (Fed. Cir. 1990)). Mehta, however, does not teach the elements arranged as required by the claim.

Even if the claimed subject matter could be divined from Mehta, it is well established that picking and choosing from different portions of a reference does not constitute anticipation. *See*, *In re Arkley*, 455 F.2d 586, 587 (CCPA 1972) (reversing the Examiner's 35 U.S.C. §102 rejection because the single Flynn reference did not clearly and unequivocally disclose the invention "without any need for picking, choosing, and combining" various portions of the reference that were directly related to each other); *see also*, *In re Wiggins*, 488 F.2d 538, 543 (CCPA 1973) (reversing the Examiner's 35 U.S.C. §102 rejection because the compounds, though named in the asserted reference, were not actually prepared). Instantly, the Office has given no rationale for the "picking and choosing" of portions of the Mehta reference, or how the portions would logically be assembled to anticipate the instant claims.

The instant specification also explains how to use the composition to form compounds with the desired properties: properties completely counter to those taught by Mehta. Mehta, in contrast to the Applicant's invention, has a laundry list of seven paragraphs of compounds that may be "high temperature film forming polymers." *See*, Mehta from Col. 4, l. 24 – Col. 5, l. 55.

Applicant submits that although these compounds are named in the reference, there is no evidence that the compounds were actually prepared and have the properties of the instantly claimed dosage forms. The picking and choosing from the laundry list of compounds by the Examiner does not constitute anticipation.

In addition, Applicant submits that Mehta cannot anticipate the current claims because Mehta is so vague and obtuse that it is unclear which compounds are “high” or “low” temperature film forming polymers and how they are to be combined and/or used. For example, Mehta states an example of a high temperature film-forming polymer is Eudragit E100. *See*, Mehta at col. 5, l. 18. Mehta then states an example of a low temperature film-forming polymer is Eudragit E100. *See*, Mehta at col. 6, l. 6. Thus, according to Mehta, one compound can be both a high temperature and low temperature film-forming polymer. This lack of clear delineations between the polymers of Mehta, combined with picking and choosing by the Examiner, further combined with Examiner’s hindsight, would thus still not result in the elements of the claims arranged as required by the claims.

In conclusion, Mehta does not anticipate independent Claim 16 or any of their dependent claims because it does not anticipate each and every element as set forth in the claims. For example, Mehta does not teach use of solubilizing agent. Further, Mehta does not anticipate the instant claims or any of their dependent claims because the picking and choosing of compounds from Mehta, with use of hindsight, does not constitute anticipation. As Claims 17, 19 – 31 contain the limitations from independent Claim 16, Mehta cannot anticipate the dependent claims. Thus, the Applicant respectfully requests the Examiner withdraw the 102 rejection.

The Applicants, therefore, respectfully request that the rejection to Claims 16 – 26 and 28 – 31 under 35 U.S.C. § 102(b) be withdrawn.

### **REJECTION UNDER 35 U.S.C. § 103**

The factual inquires set forth in *Graham v. John Deere Co.*, 383 U.S. 1,148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

- (1) Determining the scope and contents of the prior art.
- (2) Ascertaining the differences between the prior art and the claims at issue.
- (3) Resolving the level of ordinary skill in the pertinent art.
- (4) Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 16-31 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Mehta (U.S. 5,084,278), in view of Mulye (U.S. 6,946,146).

Applicants respectfully traverse this rejection as Mulye does not cure the deficiencies of Mehta. For instance, as noted above, Mehta does not teach use of a solubilizing agent in the core, which is required by the instant claims. Mulye does not cure this deficiency as Mulye also does not teach a solubilizing agent in the core.

As Claims 17, 19 – 31 contain the limitations from independent Claim 16, Applicants respectfully request that the rejection to Claims 16 – 17, 19 – 31 under 35 U.S.C. § 103(a) be withdrawn.

### **CONCLUSION**

In view of the above remarks and amendments, the Applicants respectfully submit that each of the pending objections and rejections has been addressed and overcome, placing the present application in condition for allowance. A notice to that effect is respectfully requested. If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to contact the undersigned.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the telephone number of the undersigned below.

Applicants submit concurrently a request for a one-month extension of time under 37 C.F.R. 1.136 and the accompanying fee. Please charge our Credit Card in the amount of \$120.00 covering the fee set forth in 37 CFR 1.136(a). Credit Card Payment Form SB-2038, with a signature from an authorized cardholder, is enclosed. In the event that any additional extension of time is necessary to prevent the abandonment of this patent application, then such extension of time is petitioned. The U.S. Patent and Trademark Office is authorized to charge any additional fees that may be required in conjunction with this submission to Deposit Account Number 50-2228, under Order No. 022290.0123PTUS from which the undersigned is authorized to draw.

Respectfully submitted,

Dated: May 13, 2008

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